

Remarks

Claims 16-55, 81 and 82 are pending.

§ 103 Rejection over Boyer

Claims 16-25, 32-34, 36-45, 52-54, 81 and 82 are rejected under 35 U.S.C. § 103 as being obvious over Boyer (U.S. Patent No. 4,800,079).

Applicants respectfully traverse the rejection and respectfully submit that Boyer does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36.

Boyer discloses a composition containing micronized fenofibrate, a polymer such as polyvinylpyrrolidone (PVP), and possibly starch. The sole example that is provided in Boyer¹ comprises 400 kg of fenofibrate and 20 kg of PVP and/or methacrylate. As correctly pointed out by the U.S. Patent Office (PTO), Boyer's ratio of fenofibrate to polymer is about 20:1². Boyer does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to PVP of 20:1 to be any where near the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Boyer is significantly different than the claimed weight ratio and there is no motivation or suggestion to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Boyer has more than 5 times fenofibrate to PVP than the claimed ratio of fenofibrate to polymer.

One skilled in the art could not use routine experimentation to arrive at the claimed ratio because it would require one to drastically reduce Boyer's ratio to be 5 times less than stated to arrive at the claimed invention. Routine variation or experimentation would revolve around Boyer's ratio of 20:1, and not the claimed ratio that is 5 times smaller. In view of the significant difference in the ratios, the claimed ratio is not encompassed by Boyer and is not merely an optimization of the ratio described by Boyer.

In the section "Response to Arguments", the Examiner has stated that:

"It remains the position of the Examiner that such claimed ratios are attainable by one of ordinary skill in the art through routine or

¹ Boyer at column 3.

² A correct calculation is 400kg of fenofibrate for 15kg of polymer, since 5 kg out of 20 are used for the coating. The value for 400:15 is higher than 20:1, and is about 27:1.

manipulative experimentation to obtain optimal results. The claimed ratios, which; albeit are reduced weight ratios in comparison with Boyer, who teaches a fenofibrate to polymer ratio of 20:1, nonetheless, do not render a patentable distinction over the explicit reference teachings. [...] The argument that "the sole example in Boyer comprises 400kg of fenofibrate and 20kg of PVP and/methacrylate (20:1 ratio) was not persuasive since the teaching of the prior art are not limited to the examples demonstrated therein. The reference as a whole is being considered for what it explicitly teaches."

The Examiner erred in this finding. Indeed, Boyer uses a very specific process. Boyer's process uses a solution of polymer in alcohol (95°), where the polymer concentration is 12.5% by weight. Boyer at column 2, lines 52-55.

"Thereafter, the inert cores are rotated in a turbine and they are dampened with an alcohol solution containing 12.5% by weight of a methylacrylic polymer (95.degree. alcohol)."

For 20kg of polymer, this will generate a total volume of alcoholic composition of 160kg. Thus, Boyer uses a rather high amount of alcoholic composition for the manufacture of a dosage form comprising 200kg of fenofibrate. The question is whether the skilled man would have changed Boyer and made manipulative experimentation towards the claimed ratios. The answer is necessarily negative. Using five times more polymer, i.e. use a fenofibrate to polymer ratio of 4:1, would necessarily require five times more alcohol. Thus, to manufacture a dosage form having a fenofibrate to polymer ratio of 4:1 and comprising 200kg of fenofibrate, about 800kg of alcohol would be needed. This is obviously not a technical solution that would be implemented by a man skilled in the art. The alcoholic solution in Boyer is evaporated off from the turbine. See Boyer at column 2, lines 64-67:

"The grains are then immediately dried very rapidly in order to prevent the alcohol from having enough time to dissolve the fenofibrate (a flow of air is passed through the turbine)."

This means that the entire alcoholic solvent is evaporated off "very rapidly". This appears to be mandatory in the Boyer process, so as to prevent dissolution of fenofibrate. Thus, it is a requisite of the Boyer process that the solvent must be able to be evaporated off very rapidly. This requirement hinders the use of high amounts of alcohol, since this will not allow

evaporating the solvent (using an air flow) in a sufficiently short period of time. Thus, the skilled man would not increase the amount of alcohol in the process of Boyer. Because he skilled man would not increase the amount of alcohol, he would also not increase the amount of polymer dissolved in the alcohol composition. The skilled man thus simply cannot arrive at the invention starting from Boyer.

Further, the invention recites a disintegrating agent. Such an agent is absent in the disclosure of Boyer. Thus, the skilled man simply cannot achieve the present invention because one integer of the claim is absent from the cited prior art document.

Last, Applicant has provided a declaration by Reginault (the Reginault declaration). In the Reginault declaration the Boyer composition is compared to the instant invention. The conclusion is that the presently claimed invention has an unexpectedly superior dissolution profile when compared to Boyer. This point is apparently not contested by the Examiner, which only indicates:

“Applicant’s argument that “the instant invention provides an unexpectedly superior profile when compared to Boyer” was not persuasive since dissolution profiles are not what are being claimed herein.”

The Examiner however failed to recognize that dissolution profiles can be achieved thanks to the invention. By comparing dissolution profiles, one compares what can be achieved by the invention and the prior art. The Reginault declaration thus provides a valuable comparison between Boyer and the invention, which is a showing of the superiority of the present invention over Boyer.

§ 103 Rejection over Curtet

Claims 16-55, 81 and 82 are rejected under 35 U.S.C. § 103 as being obvious over Curtet et al (U.S. Patent No. 4,895,726).

Applicants respectfully traverse the rejection and respectfully submit that Curtet does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1, as recited in independent claims 16 and 36, nor the presence of a disintegrant.

The hydrophilic polymers in the present invention are used in addition to disintegrating agents. For example, polyvinylpyrrolidone (PVP) and cross-linked polyvinylpyrrolidone (X-PVP) are different materials exhibiting different properties. For example, in one embodiment, the invention uses PVP as the hydrophilic polymer and X-PVP as the disintegrating agent (see examples section). The claimed invention used both a hydrophilic polymer and a disintegrating agent.

Curtet fails to disclose the presence of both a hydrophilic polymer and a disintegrating agent, because Curtet uses only a cross-linked PVP (i.e., a disintegrating agent). One skilled in the art would recognize that Curtet's cross-linked PVP is not a hydrophilic polymer within the meaning of the invention because the specification of the present invention teaches that it is a disintegrating agent.

Assuming, *arguendo*, the cross-linked PVP used in Curtet is a polymer of the present invention (which it is not), the cited references still do not disclose or suggest the claimed weight ratios of fenofibrate to polymer of between 1:10 and 4:1.

Curtet provides working examples comprising 200 grams fenofibrate and 7 grams cross-linked polyvinylpyrrolidone,³ such that the weight ratio of fenofibrate to cross-linked polyvinylpyrrolidone is 29:1. Curtet does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to cross-linked polyvinylpyrrolidone (PVP) of 29:1 in Curtet to fall within the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Curtet is significantly different than the claimed weight ratio and there is no motivation or suggestion in any of the references to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Curtet has greater than 7 times more fenofibrate to cross-linked PVP than the claimed ratio of fenofibrate to polymer. There is simply no motivation in any of the references to drastically reduce the ratio used in Curtet to arrive at the claimed invention.

The PTO asserts that Applicants failed to establish a patentable distinction, which accrues from the claimed weight ratios of fenofibrate to polymer. Applicants respectfully disagree. Applicants noted the PTO's comments in the section "Response to Arguments" but

³ Curtet at column 2, lines 30-40 and column 2, line 65 to column 3, line 5, assuming, *arguendo*, that cross-linked PVP is a hydrophilic polymer (which it is not).

note that the Blouquin Declaration was not commented on by the Examiner.⁴ The Blouquin Declaration shows, in addition to the data presented in the application,⁵ the criticality of the claimed ratio. As far as the showing and the relevancy of the declarations, Examiner's attention is drawn to the conclusion in the section above for Boyer.

Applicants respectfully submit that Curtet does not disclose a composition comprising both a hydrophilic polymer and a disintegrating agent; and the Bloquin Declaration and examples demonstrate the criticality of the claimed ratio of fenofibrate to polymer.

Summary

An early and favorable reconsideration and allowance of claims 16-55 and 81-82 is respectfully requested.

Respectfully submitted,



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⁴ See the response dated September 6, 2006 at page 6, last paragraph and page 7.

⁵ See the response dated January 26, 2007 at page 7, second and third full paragraphs.